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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,159	09/01/2005	Linda Li Xiao	072121-0397	1853

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EXAMINER	
HUANG, GIGI GEORGIANA	
ART UNIT	**PAPER NUMBER**
1618	

MAIL DATE	DELIVERY MODE
12/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/505,159	XIAO ET AL.	
	Examiner	Art Unit	
	GiGi Huang	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :8/20/2004, 8/20/2004, 11/29/2004, 3/30/2005, 4/6/2005, 6/13/2005, 11/28/2006.

DETAILED ACTION

Status of Application

1. Claims 1-19 are present for examination at this time.

Information Disclosure Statement

2. The information disclosure statement filed November 28, 2006 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because EP 0 571 921 has no translation. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him.

For a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. A written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, or chemical name of the claimed subject matter sufficient to distinguish it from other materials.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic.

Lee et al. (U.S. Pat. No. 6287763) addresses the role of MC4-R in the regulation of body weight and teaches the concept of at least three different assay systems to identify compounds or composition that modulate MC4-R activity or MC4-r gene expression to modulate weight control (Col. 9, lines 54-68, Col. 10, lines 1-68, Col. 11, lines 1-68, Col. 12-16, lines 1-68, Col.17, lines 1—37). As a result, not all melanocortin-4 receptors agonists are known.

As stated supra, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claims 1-18 are broad and generic, with respect to all possible compounds encompassed by the claims. The possible structural variations are limitless to any combination of compounds including proteins. Although the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond those compounds specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of the compounds identified in the specification table 3 and/or examples, the specification does not provide sufficient descriptive support for the myriad of compounds embraced by the claims.

5. Claims 1-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the thirteen compound species in Table 3 (pages 24-27), does not reasonably provide enablement for delivery methods for all melanocortin-4 receptors agonists. The specification does not enable any person skilled

in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The invention provides for nasal delivery of all compounds that can provide an agonistic function at melanocortin-4 receptor sites.

(2) The state of the prior art

The state of melanocorting-4 receptor agonists comprises various types of molecules from peptide moieties to small molecule compounds that contain guanidine group. Lee et al. (U.S. Pat. No. 6287763) addresses the role of MC4-R in the regulation of body weight and teaches the concept of at least three different assay systems to identify compounds or composition that modulate MC-R4 activity or MC$-r gene expression to modulate weight control, and to measure the amount of expression and/or activity to be useful (Col. 9, lines 54-68, Col. 10, lines 1-68, Col. 11, lines 1-68, Col. 12-16, lines 1-68, Col.17, lines 1—37). As a result, not all melanocortin-4 receptors agonists are enabled for the methods.

(3) The relative skill of those in the art

The relative skill of those in the art is high and includes pharmaceutical scientists with a through understanding of organic and medicinal chemistry as well as pharmacology, and drug delivery pharmaceutics.

(4) The predictability or unpredictability of the art

The unpredictability of functional capacity of medicinal compounds is very high. Specifically in the instant case, a common core or a common structural activity does not represent the entire genus of melanocortin-4 receptors. Accordingly, predicting their clinical efficacy is not predictable absent a painstaking experimental study.

(5) The breadth of the claims

The claims are very broad. The genus of melanocortin-4 receptors, as described in the Information Disclosure Forms of record, include such unrelated and vast group of compounds that can encompass millions of unrelated compounds.

(6) The amount of direction or guidance presented

The specification provides for specific compounds that can provide agonistic function at melanocortin-4 receptors. However, claim 1 place a functional language at the point of novelty without adequately describing the entire genus of compounds. Attention is directed to *General Electric Company v. Wabash Appliance Corporation et al,* 37 USPQ 466,469, (US 1938), speaking to functional language at the point of novelty as herein employed: "the vice of a functional claim exists not only when a claims is "wholly" functional, if that is ever true, but when the inventor is painstaking when he recites what has already been seen, and then uses conveniently functional language at the exact point of novelty". Also similar remarks are made in *University of California v. Eli Lilly:.* stating this usage does "little more than outline goals appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate." *University of Califomia v. Eli Lilly and Co.* 43 USPQ2d 1398, 1406 (CAFC 1997).

In the instant case, as herein employed by Applicants, the limitations set forth in claim 1 is directed to a functional language at the point of novelty which fails to meet the requirements set forth under 35 USC 112, first paragraph. Claims employing functional language at the point of novelty, such as Applicants' neither provides those elements required to practice the inventions, nor "inform the public during the life of the patent of the limits of the monopoly asserted." *General Electric Company v. Wabash Appliance Corporation, supra* at 468. Claims are thus Viewed to reach through time, yet provide no guidance as to the compounds or medicaments employed, levels for providing therapeutic benefit, or provide notice for those practicing in the art, or limits of protection. Simply stated, the functional limitation as appears in the instant claims is an invitation to experiment, and fails to recite a specific set of compound useful for practicing the instant invention

(7) The presence or absence of working examples

As stated above, the specification disclose guanidine containing compounds with specific characteristics in their structure. The specification does not enable the entire genus of melanocortin-4 receptor agonists.

(8) The quantity of experimentation necessary

Since the chemical characteristics of the described compounds are not representative of the entire genus of melanocortin-4 receptors, one cannot predict the mechanisms of actions and suitable delivery formulations of such compounds and thus must be burdened on a case to case basis with painstaking experimental studies that determine clinical, pharmacological and pharmaceutical properties of each formulation. Thus, when the above factors are weighed together, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine all of the compounds that provide a melanocortin-4-receptor agonist and their effective nasal delivery systems.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 3-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Bakshi et al. (WO 2000/74679).

Bakshi teaches method of delivering melanocortin-4 receptor agonists to treat various diseases mediated by such receptors including obesity and diabetes. Bakshi also teaches methods of delivery of such compounds in a suitable pharmaceutical composition including nasal preparations. Such compositions can be in the form of spray, drops, and other forms prepared by any of the methods well-know in the art of pharmacy. Nasal administration inherently occurs though olfactory epithelium as epithelial tissue is located inside the nasal cavity. The limitations regarding dosing had

been met since as no actual dosage range is claimed (Abstract, Page 4, lines 18-35, Page33, lines 3-35, Page 34, lines 1-35).

All the critical elements are taught by the cited reference and thus the claims are anticipated.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

9. Claims 1-19 are rejected under 35 U.S.C. 102(e) as being anticipated by Renhowe et al. (US Patent 6,638,927 B2).

Renhowe et al. teaches the concept of melanocortin-4 receptor agonists, the relationship of the receptor to certain conditions, specifically obesity and type II diabetes, and a method of treating an MC4-R mediated disease, comprising administering to a human subject (col. 25, line 21), melanocortin-4 receptor agonists

(Col. 1, lines 15-23, Col. 6, lines 20-33, Col. 76, lines 45-60, claims 1, 13-14). The disclosed compounds include N-{2-[2-fluoro-4-(methyloxy)phenyl]ethyl}-4[((Z)-[(3S)-3-methylpipe razin-1-yl]{[(1 S,2S, 3S, 5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]imino}methyl)amino]benzamide (example 94, col. 66, lines 25-28). The scope of formula IA and IB are identical to the compound claim. Administration via intranasal or oral formulations (col. 22, line 67), may be in the form of a solution, spray, powder, or aerosol (col. 23, lines 52-55). A therapeutically effective dose refers to that amount of the compound which results in amelioration of symptoms. Specific dosages may be adjusted depending on conditions, sex, and the diet of the subject, dose intervals, administration routes, excretion rate, and combination of drugs (col. 25, lines 1-10). Example 120 discloses administration of a MC4-R agonist in the amount of 3mg/kg for 4 weeks.

Examiner respectfully points out that administration to the upper third of the nasal cavity or olfactory epithelium is inherent because this epithelial tissue is located inside the nasal cavity and Renhowe et al. discloses intranasal administration. The limitations regarding dosing had been met since as no actual dosage range is claimed.

All the critical elements are taught by the cited reference and thus the claims are anticipated.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chu et al US patent 6,716,840.

Chu teaches method of delivering melanocortin-4 receptor agonists to treat various diseases mediated by such receptors including obesity and diabetes (see Abstract, Col 12-25; Col 26, lines 43-67). Chu teaches methods of delivery of such compounds intranasally with suitable pharmaceutical composition (Col 26, line 67; Col 27, lines 49-59). Such compositions can be in the form of spray, gels etc. (Col 27, lines 48-55). Nasal administration inherently occurs though olfactory epithelium. Chu's compounds include that of instant compounds 7 and 8 of claim 19 (Col. 38, lines 60-68, Col.39, lines 48-68). Chu meets all elemental steps of the instant claims except the specific amount of the claimed compounds when compared to its equivalent oral dose. However, absent a showing of unexpected results, it would have been obvious to one of ordinary skill in the art at the time of invention to optimize the dosing and potency of Chu's nasal formulations by routine experimentations and improve clinical benefits of such compounds.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims

are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1-19 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1, 4-20 of copending Application No. 10374507 (also U.S. Pat. Pub. No. 2003/0229025). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims disclose a method of treating an MC4-R mediated disease, comprising administering to a human in need thereof, one compound of claim 19, wherein the MC4-R mediated disease is obesity or type II diabetes.

This is a provisional obviousness-type double patenting rejection.

13. Claims 1-19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of US Patent 6,995,269. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to a method of treating an MC4-R mediated disease including obesity or type II diabetes, comprising administering

to a mammal compounds that are MC4-R agonists, which would include the compounds in claim 19.

The scope for formula IIA or IIB reads on the claims. The scope is slightly broader than the compounds in claim 19, however the instant invention is a species within the genus, since the variables, W, X, Y, Z have been defined as carbon.

Examiner notes that this is a typical genus/species situation. Once a *prima facie* case of obviousness is established, the burden is shifted to the Applicant for objective evidence for nonobviousness. See MPEP 2144.08.

Conclusion

14. Claims 1-19 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GiGi Huang whose telephone number is (571) 272-9073. The examiner can normally be reached on Monday-Thursday 8:30AM-6:00PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GH

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER